HETEROSEXUAL TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS (HIV) IN THE UNITED STATES*

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DISCUSSION about heterosexual transmission of human immunodeficiency virus (HIV) in the United States has been continuous and vigorous since the first cases of acquired immunodeficiency syndrome (AIDS) were reported in women whose only known risk factor was sexual contact with a man who had AIDS or who was at risk of AIDS.[1-4] The discussion initially focused on the question whether HIV could be transmitted by sexual contact between two heterosexual partners, with particular attention being given to the question whether female-to-female transmission could occur. Subsequently, the primary issues became the extent of heterosexual transmission occurring in the United States and the reasons for the apparently large disparity between the frequency of transmission of HIV among heterosexuals in other areas of the world—especially countries of central and eastern Africa—compared with the United States.[5-6].

This paper will review three sources of data about heterosexually transmitted HIV infection and AIDS in the United States: the cases of AIDS reported through the national AIDS surveillance program, published studies of HIV transmission among heterosexuals, and seroprevalence data about HIV infection in the heterosexual population.

SURVEILLANCE OF HETEROSEXUALLY TRANSMITTED AIDS CASES

Physicians and health departments began surveillance for cases of AIDS in 1981 following publication of the first reports of the new disease.[7] The national surveillance system was intensified in 1983 with distribution of case report forms and a formal definition of AIDS and with passage of a resolution by the Council of State and Territorial Epidemiologists to make AIDS a

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reportable condition. People with AIDS are considered to have heterosexually acquired infection if they give no history of male homosexual contact or intravenous drug abuse, do not have a clotting factor disorder requiring factor concentrate therapy, and if they report specific heterosexual contact with a person known to be infected with HIV or who has a risk factor for HIV infection. People born in such areas as Haiti or a country in central or eastern Africa where AIDS is also epidemic and heterosexual transmission is reported to be common are also classified as heterosexually transmitted cases unless they give a history of other risk factors. People who report only heterosexual contact with a prostitute or who have had multiple sex partners who are not known to be at risk for HIV infection currently are not considered to be heterosexually transmitted cases.

Cumulatively, 55,315 AIDS cases in adults and adolescents had been reported to the Centers for Disease Control between 1981 and March 14, 1988. Of these, 1,018 of 51,116 (2.0%) cases in men and 1,215 of 4,199 (28.9%) cases in women are classified as heterosexually transmitted (Table I). Only 1,307 of the 2,233 (58.5%) heterosexually transmitted cases occurred in people born in the United States; 926 (41.5%) have been reported in those born in Haiti or a country of central or eastern Africa. The trend since 1981 shows a slowly increasing number of cases in this latter group compared with a much more rapidly rising number of cases in people born in the United States (Table II). The proportion of men with AIDS who give a history of specific sexual contact with a person at risk of AIDS/HIV infection has increased from 0.2% of cases diagnosed before 1983 to 0.9% of those diagnosed in 1987, and the proportion of women has increased from 14.6 to 25.4% over the same period. Projections of future trends of the AIDS epidemic suggest that the proportion of cases in people with heterosexually transmitted AIDS born in the United States will increase from the combined proportion of 3.1% recorded in 1987 to 5.0% (68% confidence bounds, 3.6%-6.8%).[8] In contrast, the proportion of AIDS cases among people born in other countries in which heterosexual transmission of HIV is common has decreased from 5.3% of men and 12.2% of women to 1.0% and 3.8% respectively between 1981 and 1987.

Risk factors of the sexual contacts. For both men and women with heterosexually transmitted AIDS born in the United States, approximately two thirds of the sexual contacts or index partners were intravenous drug abusers (Table III). For women, bisexual men were the second most common contact, while for men about 25% of cases gave a much less specific history of contact with a person with AIDS or HIV infection or with a person of

TABLE I. RISK FACTORS FOR ADULTS WITH AIDS,* BY SEX

Risk factor	*Males*		*Females*		*Total*	
Homo/bisexual Male	39,691	(77.6)	—	(—)	39,691	(71.8)
No IV-drug use	35,577	(69.6)	—	(—)	35,577	(64.3)
IV-drug use	4,114	(8.0)	—	(—)	4,114	(7.4)
Heterosexual person	10,666	(19.7)	4,199	(100.0)	13,906	(25.1)
IV-drug use	7,631	(14.9)	2,136	(50.9)	9,767	(17.7)
Hemophilia	543	(1.1)	22	(0.5)	565	(1.0)
Sexual contact	1,018	(2.0)	1,215	(28.9)	2,233	(4.0)
Transfusion	874	(1.7)	467	(11.1)	1,341	(2.4)
Risk undetermined	1,359	(2.7)	359	(8.6)	1,718	(3.1)
Total	51,116	(92.4)	4,199	(7.6)	55,315	(100.0)

*Cases diagnosed and reported through March 14, 1988

TABLE II. HETEROSEXUALLY TRANSMITTED AIDS CASES BY YEAR OF DIAGNOSIS,* REGION OF BIRTH AND SEX

Year of diagnosis	*U.S. Born*				*Non-U.S. born***				*Total*	
	Males		*Females*		*Males*		*Females*			
Pre-1983	2	(0.2)†	12	(14.6)	66	(5.3)	10	(12.2)	90	(6.8)
1983	1	(0.0)	27	(14.8)	86	(3.3)	14	(7.7)	128	(4.6)
1984	19	(0.4)	62	(17.7)	105	(2.0)	22	(6.3)	208	(3.7)
1985	33	(0.3)	157	(23.1)	121	(1.3)	36	(5.3)	347	(3.4)
1986	76	(0.5)	306	(26.9)	158	(1.1)	56	(4.9)	596	(3.9)
1987	157	(0.9)	427	(25.4)	179	(1.0)	64	(3.8)	827	(4.3)
1988	7	(0.8)	21	(25.0)	8	(0.9)	1	(1.2)	37	(3.7)
Total	295	(0.6)	1,012	(24.1)	723	(1.4)	203	(4.8)	2,233	(4.0)

*Cases diagnosed and reported through March 14, 1988
**Cases born in a country in which heterosexual transmission of HIV is reported to be common
†Percentage of all AIDS cases diagnosed that year by sex

TABLE III. HETEROSEXUALLY TRANSMITTED AIDS CASES: REPORTED SEXUAL CONTACTS FOR U.S. BORN CASES, BY SEX*

Sexual contact	*Males*		*Females*		*Total*	
Bisexual males	—	(—)	161	(15.9)	161	(12.3)
IV-drug user	196	(66.4)	696	(68.8)	892	(68.2)
Person with hemophilia**	2	(0.7)	18	(1.8)	20	(1.5)
Immigrant to U.S.	17	(5.8)	20	(2.0)	37	(2.8)
Transfusion recipient	5	(1.7)	19	(1.9)	24	(1.8)
Person with HIV/AIDS†	43	(14.6)	80	(7.9)	123	(9.4)
Risk undetermined‡	32	(10.8)	18	(1.8)	50	(3.8)
Total	295	(100.0)	1,012	(100.0)	1,307	(100.0)

*Cases diagnosed and reported through March 14, 1988
**Person with congenital clotting disorder treated with clotting factor concentrates
†Person reported to be the sexual contact was stated to have AIDS or to be infected with HIV but a specific risk factor was not reported through the surveillance system
‡Risk factor for the sexual contact was not reported through the surveillance system and is still under investigation

undetermined risk. Black and Hispanic people with heterosexually transmitted AIDS were more likely than whites to report an intravenous drug abuser as their sex partner (for men, 71% and 77% compared with 57%, respectively; for women, 75% and 84% compared with 46% respectively; $p<0.0001$ for women). For black and Hispanic women, the cumulative incidence of AIDS through heterosexual contact with an intravenous drug abuser is more than 24 times that for white women.[9] In contrast, white women with heterosexually transmitted AIDS were approximately three times as likely as black or Hispanic women to report a bisexual man as their sexual contact (30% compared with 11% and 8% respectively; $p<0.0001$).

Little information is available about specific risk factors for immigrants with AIDS classified by place of birth in a country where heterosexually transmitted HIV infection is common. A case-control study of Haitian immigrants with AIDS concluded that heterosexual contact was the most likely means of HIV infection, although specific partners were rarely implicated.[10] This information is corroborated by studies in Africa and Haiti that suggest a high frequency of heterosexual transmission of HIV in those areas.[5,11] Another risk association for AIDS in Haitians living in the United States is migration from Haiti since 1977, which is probably related to a high prevalence of HIV infection in the large population of "boat people" who immigrated to the United States in the late 1970s and early 1980s.[10,12]

Geographic distribution of the AIDS cases. Geographically, 67% of all heterosexually transmitted AIDS cases have occurred in only four states: New York (29.7% of these cases), Florida (25.5%), New Jersey (12.1%), and California (6.0%) (Table IV). These same states have reported 65% of the heterosexually transmitted AIDS cases born in the United States, while New York, Florida, New Jersey, and Massachusetts have reported 90% of all the AIDS cases in those born in other countries in which heterosexual transmission of HIV is common. As with other cases of AIDS, most heterosexually transmitted cases have occurred among residents of major metropolitan areas. The ratio of men to women among the cases born in the United States ranges from approximately 0.2:1 to 0.5:1 in most states, but two prominent exceptions are from among the states that have reported the most cases. New York has reported more than 25 times as many heterosexually transmitted cases in women as in men, giving a male-to-female ratio of only 0.04:1 while Florida has reported almost equal numbers of cases in men and women, yielding a ratio of 0.9:1. In contrast to New York, New Jersey has reported only four times as many cases in women as in men even though most metropolitan areas in which the heterosexually transmitted AIDS cases have oc-

TABLE IV. HETEROSEXUALLY TRANSMITTED AIDS CASES BY STATE OF RESIDENCE,* REGION OF BIRTH AND SEX

State of residence	*U.S. born*				*Non-U.S. born***				*Total*	
	Males		*Females*		*Males*		*Females*			
New York	14	(0.1)†	363	(23.0)	229	(1.8)	58	(3.7)	664	(4.7)
Florida	75	(2.2)	79	(19.3)	309	(9.0)	107	(26.2)	570	(14.8)
New Jersey	40	(1.3)	161	(23.0)	57	(1.9)	12	(1.7)	270	(7.4)
California	41	(0.3)	82	(28.2)	10	(0.1)	2	(0.7)	135	(1.1)
Massachusetts	7	(0.7)	27	(24.5)	52	(4.9)	13	(11.8)	99	(8.4)
Illinois	4	(0.3)	14	(23.0)	17	(1.2)	1	(1.6)	36	(2.3)
Maryland	9	(1.0)	26	(27.7)	13	(1.5)	3	(3.2)	51	(5.3)
Connecticut	10	(1.8)	22	(21.4)	7	(1.3)	1	(1.0)	40	(6.2)
Pennsylvania	4	(0.3)	25	(29.1)	7	(0.5)	1	(1.2)	37	(2.6)
Texas	11	(0.3)	21	(22.6)	2	(0.1)	1	(1.1)	35	(0.9)

*All states and territories with ≥30 heterosexually transmitted cases diagnosed and reported through March 14, 1988

**Cases born in a country in which heterosexual transmission of HIV is reported to be common

†Percentage of all AIDS cases in that state by sex

curred are within a relatively short distance of New York City. Reasons for these differences are not apparent from surveillance reports.

Race/ethnic group of the AIDS cases. The racial and ethnic group distribution of heterosexually transmitted AIDS cases born in the United States shows a dominance of cases in black and Hispanic populations (Table V). Compared with the distribution of all AIDS cases, the proportion of black men with heterosexually transmitted infection is more than twice as high, while that of Hispanic men is about the same; among women the distribution approximately parallels that of all AIDS cases. The relative risk of heterosexually transmitted AIDS is 11.3 and 12.6 respectively for black men and women older than 16 in the United States compared with 4.6 and 13.1 for Hispanic and 1.0 for white men and women. The racial distribution of AIDS cases in people born in other countries in which heterosexual transmission of HIV is common is predominantly black, reflecting the countries of origin of these people.

Age distribution of the AIDS cases. For men the age distribution of heterosexually transmitted AIDS cases born in the United States (Table VI) is similar to that of all AIDS cases except that it does not peak so sharply during the fourth decade of life and a larger percentage is diagnosed after the age of 49 (19.7% for the heterosexually transmitted cases compared with 10.3% for all other cases). The difference in age distribution at time of diagnosis between men and women with heterosexually transmitted AIDS is statistically highly significant ($p = 0.0001$). In contrast to the men, the age distribution of heterosexually transmitted cases in women is shifted to a younger age at

TABLE V. HETEROSEXUALLY TRANSMITTED AIDS CASES BY RACE AND ETHNIC GROUP*

Race or ethnic group	*U.S. born*				*Non-U.S. born***			
	Males		*Females*		*Males*		*Females*	
White	108	(36.6)	282	(27.9)	2	(0.3)	0	(0.0)
Black	151	(51.2)	475	(46.9)	715	(98.9)	199	(98.0)
Hispanic	35	(11.9)	249	(24.6)	5	(0.7)	3	(1.5)
Other	1	(0.3)	6	(0.6)	1	(0.1)	1	(0.5)
Total	295	(100.0)	1,012	(100.0)	723	(100.0)	203	(100.0)

*Cases diagnosed and reported through March 14, 1988
**Cases born in a country in which heterosexual transmission of HIV is reported to be common

TABLE VI. HETEROSEXUALLY TRANSMITTED AIDS CASES* BY AGE GROUP, REGION OF BIRTH, AND SEX

Age group (years)	*U.S. born*				*Non-U.S. born***			
	Males		*Females*		*Males*		*Females*	
13-19	1	(0.3)	10	(1.0)	4	(0.6)	3	(1.5)
20-29	64	(21.7)	384	(37.9)	256	(35.4)	87	(42.9)
30-39	109	(36.9)	422	(41.7)	335	(46.3)	91	(44.8)
40-49	63	(21.4)	115	(11.4)	97	(13.4)	11	(5.4)
50-59	36	(12.2)	57	(5.6)	24	(3.3)	7	(3.4)
≥60	22	(7.5)	24	(2.4)	7	(1.0)	4	(2.0)

*Cases diagnosed and reported through March 14, 1988
**Cases born in a country in which heterosexual transmission of HIV is reported to be common

diagnosis compared with all cases in women; almost 39% of heterosexually transmitted cases have been diagnosed before the women are 30 years old. Other analyses of the AIDS surveillance data have shown that women with heterosexually transmitted infection have a younger mean age at diagnosis than do women with other risk factors (including intravenous drug abuse) or for men with any risk factor.[13] The age distribution by race and ethnic group is similar for men but shows that white women with heterosexually transmitted AIDS tend to be slightly older than black or Hispanic women ($p = 0.001$).

People with AIDS born in other countries in which heterosexual transmission of HIV is common tend to be younger than those born in the United States; in men, the difference is statistically highly significant ($p = 0.0001$).

HIV Transmission Among Heterosexuals: Published Studies

Little question exists today about the biologic plausibility of HIV transmission during heterosexual intercourse. HIV has been isolated from semen in men[14] and from the cervical and vaginal secretions of women during various phases of the menstrual cycle;[15-17] the data, however, suggest that the pres-

ence of HIV may be intermittent.[16,17] An animal model using chimpanzees has demonstrated that swabbing virus in culture onto the vaginal mucosa results in infection, although swabbing the virus on oral mucosa (followed by brushing the animal's teeth) did not.[18] Similar studies have not been done to evaluate the susceptibility of male urethral mucosa or other genital surfaces to infection with HIV.

Published studies of HIV transmission among heterosexuals have been reviewed recently.[5,6,19,20] Among sexual partners who denied risk factors or means of HIV infection other than heterosexual contact with a known infected partner, the cumulative probability of infection varies from approximately 10% to 50%. The risk of heterosexually transmitted HIV infection consistently has been lowest (10% or less) for women who were sexual partners of men with hemophilia, even with years of regular sexual contact after infection of the men.[20-24] Others have found a higher rate of infection for the same group (21%),[25] and preliminary studies from one group suggest that the risk of transmission from a hemophilic man to his sex partner increases as the HIV infection progresses.[26] This study found that the risk of infection correlated with severe depletion of T-4 lymphocytes (50% of 10 sex partners were seropositive) and clinical illness in the man (43% of seven sex partners of men with AIDS were seropositive).

The risk of HIV transmission to sexual partners of those infected through transfusion was found to be 18% (10 of 55) in women and 8% (2 of 25) in men a mean of 2 years after the index person was infected.[27] Although the rates of infection may suggest a higher frequency of transmission from men to women than the reverse, the difference is not statistically significant. Others have observed slightly higher rates of infection.[20, 25] Infection was not associated with duration of exposure, number of sexual contacts, or type of sexual contacts; although most of the partners remained uninfected after repeated (often several hundred) sexual contacts, HIV infection was documented in several sex partners after only a limited number of contacts. Seropositive sexual partners tended to be older than those who remained seronegative.

Studies that include sexual partners of HIV-infected men who were bisexual or who had used intravenous drugs show mixed rates of infection generally higher than those of female partners of men with hemophilia. A study of women in San Francisco documented HIV infection in 22% (12 of 55) of those whose sexual partners were bisexual and 42% (5 of 12) of those whose partners were intravenous drug abusers.[25] Inexplicably, none of 7 women whose sex partners had both risk factors were infected. Because of the small

number in each group, however, the observed differences in rates of infection are not statistically significant.

Several studies have described risks of HIV infection to the sexual partners of those with AIDS. In Florida a study of 45 sexual partners of heterosexual men and women with AIDS showed that 53% (9 of 17) of the men and 14% (4 of 28) of the women were seropositive at the start of the study.[28] Of the sexual partners seronegative at enrollment in the study, 38% (3 of 8) of the men and 42% (10 of 24) of the women seroconverted during the one-to-three year period of evaluation, giving a total infection rate at the end of the study of 71% of the male and 50% of the female partners. Risk factors for infection in the index contacts were reported as birth in Haiti (17 people), intravenous drug abuse (9), bisexual male (4), blood transfusion (4), hemophilia (2), and heterosexual contact (9, including 3 women with a history of prostitution, 2 men with a history of prostitute contact, and 4 women whose former heterosexual partner reportedly was infected). The rate of infection in the studied sexual partners was 50% or higher for all risk factors except hemophilia. In New York City men and women who were steady sexual partners of patients with AIDS or related conditions were evaluated prospectively; 58% (7 of 12) of the men and 47% (41 of 88) of the women were seropositive.[29] A report from the U.S. Army described HIV infection in 5 of 7 (71%) wives of military personnel with AIDS.[30] None of the wives had a risk factor other than sexual contact with her husband; the risk factors most often reported for the husbands were intravenous drug abuse or multiple heterosexual partners, including prostitutes.

Another study from Edinburgh of sexual partners of HIV-infected people, most of whom were intravenous drug abusers and none of whom had AIDS, showed that the risk of heterosexual infection was almost equal—14% (1 of 7) in male and 15% (5 of 35) in female sexual partners.[31] All the couples were reported to have been in steady relationships.

None of the studies has been able to delineate clearly the major risk factors or variables that influence transmission of HIV between heterosexual sex partners. Anal and oral sexual activity have been associated with a higher risk of HIV transmission among heterosexual people in some studies[25,28,29] but not in others.[25,27,32] Neither is necessary for transmission to either men or women. Intercourse during menses has been associated with an increased risk of infection to women in one study[32] but not in others.[25,29] Several studies noted that total number of sex partners (without regard to infection status of the partners) was not associated with a higher risk of infection.[10,25,32] Most

also found no relationship between the number of sexual contacts and the risk of infection from a known infected partner,[26-29] but one did note a significantly higher risk of HIV infection in women reporting more than 100 contacts with their HIV-infected sexual partner.[25] In contrast, one study noted that several partners became infected after only a few sexual contacts with their infected partner.[27] The significance of the duration of the relationship also varied, with two studies noting this as an important association with infection [25,31] and others finding no association.[26,27,29]

The risk associated with genital ulcer disease, multiple partners, and prostitute contact in many of the studies in Africa[33] have not been replicated in the United States. Several studies suggest that a prior history of sexually transmitted diseases is associated with a subsequent risk of heterosexually transmitted HIV, [10, 28] but others did not find this association.[25] Most studies of heterosexually transmitted HIV infection in the United States did not comment specifically on diseases associated with genital ulcers. Several studies, however, have found that homosexual men with serologic evidence of recent herpes simplex virus type II infection and/or syphilis are at increased risk of HIV infection, suggesting that in this country also sexually transmitted diseases that disrupt cutaneous or mucosal integrity may facilitate transmission of HIV.[34,35]

The absence of consistently associated variables for transmission of HIV suggests that biologic variability either on the part of the host or the virus may be extremely important.[13,19] An additional argument in support of this is the fact that although the cumulative evidence suggests a low risk of HIV infection from a single sexual contact with an infected person, in several instances a high percentage of women exposed only occasionally to semen from a single man have become HIV infected.[36,37] This has occurred both with artifical insemination (4 of 8 women inseminated from one donor) and with vaginal intercourse (10 of 17 women who were partners of one man). For whatever reason—tissue or organ systems involved with infection, stage of infection, virulence of the viral strain—some people appear to be more capable of transmitting HIV infection to others, at least at some stage of their infection. Observations about the correlation between the disease state and the ease with which HIV can be isolated from the person are consistent with this.[38]

Prevalence of HIV Infection In Heterosexual Populations

Since the latent period between infection with HIV and diagnosis of AIDS often is years, focusing on the distribution of AIDS cases gives a crude

picture only of risks in the past at the time infection occurred. Current risks can be assessed only through studies of the incidence and prevalence of infection. Incidence studies are difficult to accomplish with an infection that is most often unrecognized clinically during the acute and early latent stages. Prevalence of HIV infection can be estimated through serosurveys, although trying to determine the prevalence in the heterosexual population of the United States in the aggregate is almost impossible. Studies conducted in selected populations, however, can provide highly useful information about the frequency of infection,[39] although the means of transmission to the infected person often cannot be determined accurately through serosurveys.

Blood donors. Blood donors have been informed since 1983 about risk factors for HIV infection and AIDS, and have been asked not to donate blood if they have a risk factor; in addition, donated units of blood have been screened for anti-HIV since the spring of 1985. The American Red Cross Blood Services collected approximately 12.6 million units of blood between April 1985 and May 1987 from more than 50 regional centers scattered across the United States. The mean frequency of blood units positive for anti-HIV was 0.02%; as seropositive donors were identified and excluded from the donor pool, the prevalence has declined from 0.035% in mid-1985 to 0.012% in mid-1987.[39] The frequency of infection among first-time blood donors has remained at a higher level, 0.043%. The rates were much higher for men than for women and for blacks and Hispanics than for whites. From 80% to 90% of seropositive donors notified of their HIV antibody status and interviewed have acknowledged a well-defined risk factor for HIV infection. In one study conducted in 3 cities with a relatively high incidence of AIDS to evaluate risks of HIV infection in seropositive donors, the frequency of positive male donors was 0.083% and that for female donors was 0.016%.[40] Only 2 of 152 (1.3%) male donors interviewed cited heterosexual contact with a person at risk as a means of infection, and 20 (13.2%) did not state a risk factor on interview; several of these men reported sexual contact with female prostitutes. Of 34 seropositive women interviewed, 15 (44.1%) reported heterosexual contact with a person at risk for HIV infection, 3 (8.8%) had other risk factors, and 15 did not state a risk factor.

Military recruit applicants. Applicants for military service have been tested for HIV antibody since October 1985.[41] Applicants are questioned about drug use and homosexual activity, both of which are reasons for exclusion from military service. Recruits for military service, therefore, would not be expected to be representative of the United States population with regard to drug use, homosexual behavior, or medical conditions such as coagulation

deficiencies even after adjusting for age, sex, and race. The crude prevalence of HIV infection was 0.15% among 1.25 million military recruit applicants tested between October 1985 and September 1987; adjusted for age, race, and sex to reflect the composition of the adult population 17 to 59 years of age, the prevalence was 0.14%.[39] The rates were approximately 3 times higher for men than women, 3 to 4 times higher for minority applicants than for whites, and increased with age to peak late in the third decade of life. Rates varied widely by geographic area, generally reflecting the incidence of reported AIDS cases; in some areas and for some age groups prevalence of infection exceeded 1.5%.[41] Little information is available about risk factors for infection in the recruit applicants, but the limited number of interviews conducted to date suggest that most of these persons have a well-described risk factor, particularly male homosexual contact or intravenous drug use.[39,42] Too few seropositive women have been evaluated to determine the frequency of heterosexual HIV infection in this group; interviews of a limited number of seropositive recruit applicants in New York City have found one woman infected through heterosexual contact with her intravenous drug user partner.[42]

Women of child-bearing age. Blood obtained from women prenatally or at delivery or collected from the umbilical cord or from newborn infants for other reasons have been used to estimate the frequency of HIV infection in parturient women.[39] In Massachusetts the prevalence of HIV infection in a population of 30,708 was estimated to be 0.21%, ranging from 0.80% in inner city areas to 0.09% in suburban and rural areas; no information was available about specific risk factors in the women.[43] At an inner city municipal hospital in New York City 12 of 602 (2.0%) women were found to be infected with HIV at delivery; 7 had a plausible risk factor by history, including multiple sexual partners in 1 woman.[44] In Jacksonville, Florida, 2 of 299 (0.7%) women who consented to HIV antibody testing during prenatal care were positive; 1 had multiple risks while the other had previously had several sexual partners from New York City.[45] Summaries of 5,244 women tested in 13 other studies conducted among women of reproductive age in 11 cities or areas of the United States, excluding New York City and Puerto Rico and excluding populations of women at known high risk, demonstrate only 19 seropositives for a cumulative prevalence of HIV infection of only 0.36%.[39] In New York City, however, several studies found rates greater than 2%, and in Puerto Rico rates among more than 3,600 women studied exceeded 1.7%.[39] Most of these studies were conducted predominantly among women in inner city areas where intravenous drug abuse is common, but the women

were not specifically included or excluded from testing because of any risk factor.

Sexually transmitted disease clinics and prostitutes. Sexually transmitted disease clinics are a useful source of information about the seroprevalence of HIV infection since they provide diagnosis and treatment for those at high risk of other sexually transmitted diseases. In studies among people without known risk factors for HIV infection on interview, seroprevalence ranged from 0 to just over 1%, the latter rates from clinics in San Diego and New York.[39] Seven areas reported data on 2,085 men who were tested, with 10 (0.48%) found positive, and 8 areas reported on 1,433 women with 4 (0.28%) found positive. Another study in sexually transmitted disease clinics in Baltimore found a rate of HIV seropositivity of 2.6% among 1,519 men who did not acknowledge a specific risk for infection and 1.6% among 1,005 women; of all seropositive patients, approximately one third of the men and nearly half the women did not acknowledge a risk for infection.[46] The method of ascertaining risk in this study was self-administered questionnaire with no reinterview of positive patients; information about risk might have been obtained more completely had direct questioning by a skilled interviewer been performed.[47] Risk of HIV infection was higher (0%-11%) among heterosexual people attending sexually transmitted disease clinics whose partners had other risk factors for infection (intravenous drug users, bisexual men or men with hemophilia).[39]

Risk of HIV infection in female prostitutes has been summarized.[5,39] Of 19 surveys in 10 states and Puerto Rico, an overall HIV infection rate of 8.0% was found among 3,656 prostitutes tested; the rates in the individual studies ranged from 0% to 45%, and situations varied from women in licensed brothels in Nevada to incarcerated intravenous drug users.[39] The relative significance of intravenous drug use compared with sexual transmission of infection could not be determined; others have noted that intravenous drug abuse is a major risk factor for HIV infection in these women, but unprotected sex (i.e., sex without a condom) with infected paying or non paying partners is also a risk.[48]

Conclusions: What Is The Risk Of Heterosexual Transmission Of HIV?

Cumulative evidence strongly suggests a significant risk of heterosexual transmission of HIV in the United States from an infected person to his or her sex partner. To date, most transmission has occurred from a person who has become infected through other risk factors—male homosexual activity in a

bisexual man, intravenous drug use, hemophilia with use of clotting factor concentrates, or transfusion. The AIDS surveillance data to date do not provide much evidence for continuing heterosexual transmission in the population, but the manner in which case data are collected and reported biases against that type of report. Unless a person knows that his partner is infected, reports of multiple heterosexual contacts as a risk factor or of contact with prostitutes will not be accepted as direct evidence of risk. The reason for not doing so is obvious; many people do not provide accurate risk factor information on the initial interview, and only persistent investigation will reveal the true risk factor.[47,49,50] In New York City, where health department personnel carefully question all people without a clear risk for infection, 63% of patients with AIDS who initially state that contact with prostitutes is their only risk factor subsequently give a history of other risk factors after further investigation.[50] Nationally, investigation of AIDS patients without identified risk factors has resulted in reclassification of most of those for whom additional information could be obtained.[51]

Scattered through the literature are reports of heterosexual transmission of HIV in which the source of infection in the index cases also was heterosexual contact.[28,30,37,51] Given the total number of AIDS cases—even of heterosexually transmitted AIDS cases—the number is not impressive. The primary risk for continued heterosexual transmission will come from those infected through other routes, especially intravenous drug use and bisexual behavior. A low frequency subcurrent of HIV infection that is strictly heterosexual without other risk factors undoubtedly will continue, but the evidence thus far does not suggest that it will attain the epidemic proportions reached in such areas as central and eastern Africa. We have time today to educate sexually active people about the precautions to take so that they can prevent infection in themselves and others, but effective prevention will depend on education and behavior modification now by those who may be at risk.

REFERENCES

1. Masur, H., Michelis, M.A, Wormser, G.P., et al.: Opportunistic infection in previously healthy women: initial manifestations of a community-acquired cellular immunodeficiency. *Ann. Intern. Med. 97*:523-29, 1982.
2. Centers for Disease Control: Immunodeficiency among female sexual partners of males with acquired immune deficiency syndrome (AIDS)—New York. *M.M.W.R. 31*:697-98, 1983.
3. Harris, C., Small, C.B., Klein, R.S., et al.: Immunodeficiency in female sexual partners of men with the acquired immunodeficiency syndrome. *N. Engl. J. Med. 308*:1181-84, 1983.
4. Pitchenik, A.E., Fischl, M.A., and Spira, T.J.: Acquired immune deficiency syndrome in low-risk patients: evidence for possible transmission by an asymptomatic carrier. *J.A.M.A. 250:*1310-12, 1983.
5. Padian, N.S.: Heterosexual transmission of acquired immunodeficiency syndrome: international perspectives and national projections. *Rev. Infect. Dis. 9*:947-60, 1987.
6. Chamberland, M.E. and Dondero, T.J.: Heterosexually acquired infection with human immunodeficiency virus (HIV). *Ann. Intern. Med. 107:*763-66, 1987.
7. Centers for Disease Control: Follow-up on Kaposi's sarcoma and *Pneumocystis* pneumonia. *M.M.W.R. 30*:409-10, 1981.
8. Morgan, W.M. and Curran, J.W.: Acquired immunodeficiency syndrome: current and future trends. *Public Health Rep. 101*:459-65, 1986.
9. Selik, R.M. and Rogers, M.F.: Relative risks of AIDS for American blacks and Hispanics. *III International Conference on AIDS*. Washington, D.C., 1987, p.77.
10. The Collaborative Study Group of AIDS in Haitian Americans: *J.A.M.A. 257*:635-39, 1987.
11. Johnson, W.D., Stanback, M.E., Deschamps, M-M., Santil, J., Jean-Charles, M., and Pape, J.W.: Natural history of HIV infection in spouses of AIDS patients. [Abstract]. *III International Conference on AIDS*. Washington, D.C., 1987, p.69.
12. Hardy, A.M., Allen, J.R., Morgan, W.M., and Curran, J.W.: The incidence rate of acquired immunodeficiency syndrome in selected populations. *J.A.M.A. 253*:215-20, 1985.
13. Allen, J.R. and Curran, J.W.: Prevention of AIDS and HIV infection: needs and priorities for epidemiologic research. *Am. J. Public Health 78*:381-86, 1988.
14. Ho, D.D., Schooley, R.T., Rota, T.R., et al.: HTLV-III in the semen and blood of a healthy homosexual man. *Science 226*:451-53, 1984.
15. Wofsy, C.B., Cohen, J.B., Hauer L.B., et al.: Isolation of AIDS-associated retrovirus from genital secretions of women with antibodies to the virus. *Lancet 1*:527-29, 1986.
16. Vogt, M.W., Witt, D.J., Craven, D.E., et al.: Isolation patterns of the human immunodeficiency virus from cervical secretions during the menstrual cycle of women at risk for the acquired immunodeficiency syndrome. *Ann. Intern. Med., 106*:380-82, 1987.
17. Blaser, M.J.: Isolation of the human immunodeficiency virus from cervical secretions during menses. *Ann. Intern. Med. 106*:912, 1987.
18. Fultz, P.N., McClure, H.M., Daugharty, H., et al.: Vaginal transmission of human immunodeficiency virus (HIV) to a chimpanzee. *J. Infect. Dis. 154*:896-900, 1986.
19. Friedland, G.H. and Klein, R.S.: Transmission of the human immunodeficiency virus. *N. Engl. J. Med. 317*:1125-35, 1987.
20. Curran, J.W., Jaffe, H.W., Hardy, A.M., et al.: Epidemiology of HIV infection and AIDS in the United States. *Science 239*:610-16, 1988.
21. Kreiss, J.K., Kitchen, L.W., Prince, H.E., et al.: Antibody to human T-lymphotropic virus type III in wives of hemophiliacs. *Ann. Intern. Med. 102*:623-26, 1985.
22. Jason, J.M., McDougal, S., Dixon G., et al.: HTLV-III/LAV antibody and immune status of household contacts and sexual partners of persons with hemo-

philia. *J.A.M.A. 255*:212-15, 1986.
23. Allain, J.-P.: Prevalence of HTLV-III/LAV antibodies in patients with hemophilia and in their sexual partners in France. *N. Engl. J. Med. 315*:517-18, 1986.
24. Centers for Disease Control: HIV infection and pregnancies in sexual partners of HIV-seropositive hemophilic men—United States. *M.M.W.R. 36*:593-95, 1987.
25. Padian, N., Marquis, L., Francis, D.P., et al.: Male-to-female transmission of human immunodeficiency virus. *J.A.M.A. 258*:788-90, 1987.
26. Goedert, J.J., Eyster, M.E., Biggar, R.J., and Blattner, W.A: Heterosexual transmission of human immunodeficiency virus: association with severe depletion of T-helper lymphocytes in men with hemophilia. *AIDS Res. Human. Retrovir. 3*:355-61, 1987.
27. Peterman, T.A., Stoneburner, R.L., Allen, J.R., et al.: Risk of human immunodeficiency virus transmission from heterosexual adults with transfusion-associated infection. *J.A.M.A. 259*:55-58, 1988.
28. Fischl, M.A., Dickinson, G.M., Scott, G.B., et al.:Evaluation of heterosexual partners, children, and household contacts of adults with AIDS. *J.A.M.A. 257*:640-44, 1987.
29. Steigbigel, N.H., Maude, D.W., Feiner, C.J., et al.: Heterosexual transmission of infection and disease by the human immunodeficiency virus (HIV). *III International Conference on AIDS*. Washington, D.C., 1987, p. 106.
30. Redfield, R.R., Markham, P.D., Salahuddin, S.Z., et al.: Frequent transmission of HTLV-III among spouses of patients with AIDS-related complex and AIDS. *J.A.M.A. 253*:1571-73, 1985.
31. France, A.J., Skidmore, C.A., Robertson, J.R., et al.: Heterosexual spread of human immunodeficiency virus in Edinburgh. *Br. Med. J. 296*:526-29, 1988.
32. Cohen, J.B., Hauer, L.B., Poole, L.E., and Wofsy, C.B.: Sexual and other practices and risk of HIV infection in a cohort of 450 sexually active women in San Francisco. *III International Conference on AIDS*. Washington, D.C., 1987, p.119.
33. Piot, P., Kreiss, J.K., Ndinya-Achola, J.O., et al.: Heterosexual transmission of HIV (editorial review). *AIDS 1*: 199-206, 1988.
34. Holmberg, S.D., Stewart, J.A., Gerber, A.R., et al.: Prior herpes simplex virus type 2 infection as a risk factor for HIV infection. *J.A.M.A. 259*:1048-50, 1988.
35. Handsfield, H.H., Ashley, R.L., Rompalo, A.M., et al.: Association of anogenital ulcer disease with human immunodeficiency virus infection in homosexual men. *III International Conference on AIDS*. Washington, D.C., 1987, p. 206.
36. Stewart, G.J., Cunningham, A.L., Driscoll, G.L., et al.: Transmission of human T-cell lymphotropic virus type III (HTLV-III) by artificial insemination by donor. *Lancet 2*:581-85, 1985.
37. Clumeck, N., Hermans, P., Taelman, H., et al.: Cluster of heterosexual transmission of HIV in Brussels. *III International Conference on AIDS*. Washington, D.C., 1987, p. 76.
38. Redfield, R.R., Wright, D.C., Khan, N.C., and Burke, D.S.: Correlation of HIV isolation rate and stage of infection. *III International Conference on AIDS*. Washington, D.C., 1987, p. 180.
39. Centers for Disease Control: Human immunodeficiency virus infection in the United States: a review of current knowledge. *M.M.W.R. 36* (Suppl. S-6):1-48, 1987.
40. Ward, J.W., Kleinman, S.H., Douglas, D.K., et al.: Epidemiologic characteristics of blood donors with antibody to human immunodeficiency virus. *Transfusion*. In press.
41. Burke, D.S., Brundage, J.F., Herbold, J.R., et al.: Human immunodeficiency virus infections among civilian applicants for United States military service, October 1985 to March 1986. *N. Engl. J. Med. 317*:131-36, 1987.
42. Stoneburner, R.L., Chiasson, M.A., Solomon, K., and Rosenthal, S.: Risk factors in military recruits positive for HIV antibody. *N. Engl. J. Med. 315*:1355, 1986.

43. Hoff, R., Berardi, V.P., Weiblen, B.J., et al.: Seroprevalence of human immunodeficiency virus among childbearing women. *N. Engl. J. Med. 318:*525-30, 1988.
44. Landesman, S., Minkoff, H., Holman, S., et al.: Serosurvey of human immunodeficiency virus infection in parturients. *J.A.M.A. 258:*2701-03, 1987.
45. Kaunitz, A.M., Brewer, J.L., Paryani, S.G., et al.: Prenatal care and HIV screening. *J.A.M.A. 258:*2693, 1987.
46. Quinn, T.C., Glasser, D., Cannon, R.O., et al.: Human immunodeficiency virus infection among patients attending clinics for sexually transmitted diseases. *N. Engl. J. Med. 318:*197-203, 1988.
47. Chiasson, M.A., Stoneburner, R., Lekatsa, A., and Walker, J.: Heterosexual transmission of AIDS in New York City. *III International Conference on AIDS.* Washington, D.C., 1987, p. 75.
48. Centers for Disease Control: Antibody to human immunodeficiency virus in female prostitutes. *M.M.W.R. 36:*157-61, 1987.
49. Potterat, J.J., Phillips, L., and Muth, J.B.: Lying to military physicians about risk factors for HIV infections. *J.A.M.A. 257:*1727, 1987.
50. Lekatsas, A., Walker, J., O'Donnel, R., et al.: Identification of risk in persons with AIDS in New York City: when is "no risk" without risk? *II International Conference on AIDS.* Paris, France, 1986, p.151.
51. Castro, K.G., Lifson, A.R., White, C.R., et al.: Investigations of AIDS patients with no previously identified risk factors. *J.A.M.A. 259:*1338-42, 1988.
52. Calabrese, L.H. and Gopalakrishna, K.V.: Transmission of HTLV-III infections from man to woman to man. *N. Engl. J. Med. 314:*987, 1986.